BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 21 April 1999 (21.04.99)	
International application No. PCT/CA98/00773	**Applicant's or agent's file reference** PCT-1034
International filing date (day/month/year) 07 August 1998 (07.08.98)	**Priority date** (day/month/year) 15 August 1997 (15.08.97)
Applicant SHERMAN, Bernard, Charles	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

10 March 1999 (10.03.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Lazar Joseph Panakal
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

2578181

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61K 31/545, 9/14, 9/20

A1

(11) International Publication Number: **WO 99/08683**

(43) International Publication Date: 25 February 1999 (25.02.99)

(21) International Application Number: PCT/CA98/00773

(22) International Filing Date: 7 August 1998 (07.08.98)

(30) Priority Data:
2,209,868 15 August 1997 (15.08.97) CA

(71)(72) Applicant and Inventor: SHERMAN, Bernard, Charles [CA/CA]; 50 Old Colony Road, Willowdale, Ontario M2L 2K1 (CA).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: PHARMACEUTICAL COMPOSITIONS COMPRISING CEFUROXIME AXETIL

(57) Abstract

A co–precipitate of cefuroxime axetil and a water–soluble excipient. Process for making said co–precipitate, and pharmaceutical compositions for oral administration comprising said co–precipitate.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

PHARMACEUTICAL COMPOSITIONS COMPRISING CEFUROXIME AXETIL

BACKGROUND

Cefuroxime axetil is an antibiotic effective against a wide spectrum of microorganisms. Antibiotics for oral administration should be in a form which provides high bioavailability, whereby absorption into the bloodstream from the gastro-intestinal tract is maximized.

For cefuroxime axetil, the prior art discloses substantial difficulties in making compositions for oral administration providing high bioavailability.

Pure cefuroxime axetil can be produced in crystalline form or amorphous form. U.S. patent 4820833 discloses that the pure amorphous form is more soluble in water than the pure crystalline form and gives higher bioavailability upon oral administration.

U.S. patent 4897270 further discloses that film coated tablets comprising cefuroxime axetil (even in amorphous form) give low levels of absorption into the blood stream unless the tablets are formulated such that, when the tablet is ingested, the film coating ruptures very rapidly and the core then disintegrates immediately.

The prior art thus teaches that good absorption from tablets comprising cefuroxime axetil can be achieved only if the cefuroxime axetil used in the formulation is in pure amorphous form and the tablets contain sufficient disintegrant to cause them to disintegrate immediately in gastro-intestinal fluid.

It is the object of the present invention to overcome these limitations disclosed in the prior art.

More specifically, one object of the present invention is to enable compositions of cefuroxime axetil for oral administration exhibiting high bioavailability without requiring use of cefuroxime axetil in pure amorphous form; and a second object of the present invention is to enable tablets for oral administration exhibiting high bioavailability without requiring that the tablets disintegrate immediately in gastro-intestinal fluid.

BRIEF SUMMARY OF THE INVENTION

It has been found that the water solubility and hence bioavailability of cefuroxime axetil can be enhanced by making a co-precipitate comprising cefuroxime axetil and a water-soluble excipient.

It has further been found that tablets made from the co-precipitate exhibit satisfactory dissolution and bioavailability even if the tablets disintegrate over a period of many minutes, instead of immediately.

DETAILED DESCRIPTION OF THE INVENTION

As aforesaid, it has been found that the water-solubility of cefuroxime axetil can be enhanced by making a co-precipitate of cefuroxime axetil with a water-soluble excipient.

The term "water-soluble excipient" will be understood to mean an ingredient having no therapeutic activity and being nontoxic (and thus suitable as an excipient) that has a solubility in water of at least 1 g per 1000 g at 20°C. The solubility will preferably be at least 1 g per 100 g at 20°C, and more preferably at least 1 g per 10 g at 20°C. Suitable water-soluble excipients will include, for example, povidone, polyethylene glycols, hydroxypropyl cellulose, methylcellulose, lactose, mannitol and sorbitol.

A preferred water-soluble excipient is povidone. The amount of the water-soluble excipient used may be from about 2% to about 60% of the total weight of the co-precipitate, preferably from about 5% to about 25%, and most preferably about 10%.

The co-precipitate is made by dissolving pure crystalline cefuroxime axetil and the water-soluble excipient in a solvent or combination of solvents and evaporating the solvent or solvents. The solvent or solvents used will preferably be a solvent or solvents in which the cefuroxime axetil and the water soluble excipient have relatively high solubility so as to minimize the amount of solvent needed.

Since cefuroxime axetil has low solubility in water, it follows that a solvent other than water must be used to dissolve the cefuroxime axetil. Of the common organic solvents; the solvent in which cefuroxime axetil is most soluble is acetone. Acetone is thus a preferred solvent.

If the solvent selected to dissolve the cefuroxime axetil is also a good solvent for the water-soluble excipient, then only this one solvent is needed to dissolve both. However, if the solvent selected to dissolve the cefuroxime axetil is not a good solvent for the selected water-soluble excipient, then a second solvent is needed to dissolve the water-soluble excipient. That second solvent may be water or another organic solvent.

If two solvents are used, they should be capable of being inter-dissolved to enable formation of a clear solution of the cefuroxime axetil and the water-soluble excipient in the combination of solvents.

A solution of the cefuroxime axetil and water-soluble excipient in the solvent or solvents may be prepared either by dissolving the cefuroxime axetil and water-soluble excipient into solvents separately and then mixing the two solutions together, or by directly adding the cefuroxime axetil and water-soluble excipient to the solvent or mixture of solvents and mixing until a clear solution is formed.

After the solution of the cefuroxime axetil and water-soluble excipient in the solvent or solvents is prepared, it is necessary to then remove the solvent or solvents to obtain a dry co-precipitate.

This may be done, for example, by evaporating the solvent or solvents in a spray drying or roller drying process, or by evaporating the solvent or solvents under vacuum.

The dried co-precipitate comprising cefuroxime axetil and the water-soluble excipient will then be further processed into a tablet.

This may be done by mixing the co-precipitate with other excipients and then processing the mixed powder into tablets on a tablet press. The other excipients will preferably include both a disintegrant and a lubricant.

The disintegrant is an ingredient which absorbs water and swells to cause the tablet to disintegrate when the tablet is immersed in gastro-intestinal fluid. Preferred disintegrants are water-insoluble cross-linked polymers, including, for example, croscarmellose sodium, sodium starch glycolate, and crospovidone.

A lubricant is needed to prevent sticking of the powder to the tooling in the tableting process. Preferred lubricants are stearic acid and metallic stearates, such as magnesium stearate.

It will be understood that, as an alternative to preparing the dry co-precipitate by evaporation of solvents and then mixing the co-precipitate with other excipients in a subsequent step, the two steps may be done together. This may be done, for example, by spraying the solution of cefuroxime axetil and the water-soluble excipient onto other excipients in a fluidized bed drying system.

The invention will be further illustrated by the following examples, which are intended to be illustrative but not limiting of the scope of the invention.

EXAMPLE 1

2000 g of acetone and 200 g of methanol were placed in a beaker. While stirring, 500 g of pure crystalline cefuroxime axetil was slowly added, and stirring was continued for about 5 minutes, until the cefuroxime axetil was fully dissolved. Stirring was continued and 50 g of hydroxy propyl cellulose was then added. Stirring was continued for another several minutes, until the hydroxy propyl cellulose was fully dissolved. The solution was then spray-dried to obtain a co-precipitate comprising 1 part hydroxpropyl cellulose to 10 parts cefuroxime axetil.

EXAMPLE 2

The following were mixed together:

co-precipitate from example 1	-	134.2 g
croscarmellose sodium	-	44.0 g
magnesium stearate	-	1.0 g
colloidal silicon dioxide	-	0.8 g
Total	-	180.0 g

The mixed powder was compacted into slugs on a tablet press. The slugs were then ground into granules, and the granules were recompressed on a tablet press into tablets of weight 900 mg.

In view of the proportions of ingredients as aforesaid, each tablet contained 671 mg of co-precipitate, which in turn contained 610 mg of cefuroxime axetil, which in turn is equivalent to about 500 mg of cefuroxime.

The tablets were tested for disintegration time using the method set out in the United States Pharmacopoeia, 23rd edition, page 1791. The disintegration time was over 30 minutes.

The tablets were also tested for dissolution as set out in the United States Pharmacopoeia, 23rd edition, page 316. The result was about 65% in 20 minutes and 90% in 60 minutes.

The dissolution specifications for cefuroxime axetil tablets on the said page 316 are 65% in 20 minutes and 80% in 60 minutes. The tablets of this example were thus found to comply with this specification, despite the relatively slow disintegration.

The dissolution specifications in the United States Pharmacopoeia are designed to ensure that tablets meeting the specifications will exhibit acceptable bioavailability.

EXAMPLE 3

2000 g of acetone and 200 g of methanol were placed in a beaker. While stirring, 500 g of pure crystalline cefuroxime axetil was slowly added, and stirring was continued for about 5 minutes, until the cefuroxime axetil was fully dissolved. Stirring was continued and 50 g of povidone was then added. Stirring

was continued for another several minutes, until the povidone was fully dissolved. The solution was then spray-dried to obtain a co-precipitate comprising 1 part povidone to 10 parts cefuroxime axetil.

EXAMPLE 4

The following were mixed together:

co-precipitate from example 3	-	132.0 g
croscarmellose sodium	-	43.6 g
magnesium stearate	-	1.0 g
colloidal silicon dioxide	-	0.8 g
Total	-	177.4 g

The mixed powder was compacted into slugs on a tablet press. The slugs were then ground into granules, and the granules were recompressed on a tablet press into tablets of weight 900 mg.

Again, in view of the proportions of ingredients as aforesaid, each tablet contained 670 mg of co-precipitate, which in turn contained 609 mg of cefuroxime axetil, which in turn is equivalent to about 500 mg of cefuroxime.

The tablets were tested for disintegration time using the method set out in the United States Pharmacopoeia, 23rd edition, page 1791. The disintegration time was about 10 minutes.

The tablets were also tested for dissolution as set out in the United States Pharmacopoeia, 23rd edition, page 316. The result was over 80% in 20 minutes and over 90% in 60 minutes.

The tablets of this example thus exhibited dissolution substantially faster than required by the United States Pharmacopoeia, again despite the fact that disintegration was not immediate.

What is claimed is:

1. A co-precipitate comprising cefuroxime axetil and a water-soluble excipient.

2. A co-precipitate as in claim 1 comprising from about 40% to about 98% by weight cefuroxime axetil and from about 2% to about 60% by weight water- soluble excipient.

3. A co-precipitate as in claim 1 comprising from about 75% to about 95% by weight cefuroxime axetil and from about 5% to about 25% by weight water-soluble excipient.

4. A co-precipitate as in claim 1 comprising about 90% by weight cefuroxime axetil and about 10% by weight water-soluble excipient.

5. A co-precipitate as in any of claims 1 to 4 wherein the water-soluble excipient is selected from the group consisting of povidone, hydroxy propyl cellulose, methycellulose, lactose, mannitol and sorbitol.

6. A process of production of a co-precipitate of any of claims 1 to 5 which comprises:-

- dissolving the cefuroxime axetil and water-soluble excipient in a solvent or a mixture of solvents; and
- evaporating the solvent or solvents.

7. A process as in claim 6 wherein acetone is used as solvent.

8. A process as in claim 6 wherein the solvent or solvents are evaporated by spray-drying.

9. A pharmaceutical tablet comprising a co-precipitate according to any of claims 1 to 5.

10. A pharmaceutical tablet as in claim 9 further comprising a disintegrant.

11. A pharmaceutical tablet as in claim 10 wherein the disintegrant is a water-insoluble cross-linked polymer.

12. A pharmaceutical tablet as in claim 10 wherein the disintegrant is selected from the group consisting of croscarmellose sodium, sodium starch glycolate and crospovidone.

13. A pharmaceutical tablet as in claim 10 further comprising a lubricant.

14. A pharmaceutical tablet as in claim 13 wherein the lubricant is stearic acid or a metallic stearate.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/CA 98/00773

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K31/545 A61K9/14 A61K9/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 757 991 A (ACS DOBFAR S.P.A.,MILAN (IT)) 12 February 1997 see the whole document ---	1-14
A	FR 2 549 837 A (GLAXO) 1 February 1985 see the whole document ---	1-14
A	EP 0 107 276 A (GLAXO) 2 May 1984 cited in the application see claims see page 23, line 1 - line 32 ---	1-14
A	GB 2 181 052 A (GLAXO) 15 April 1987 cited in the application see the whole document ---	1-14
A	GB 2 204 792 A (GLAXO) 23 November 1988 see the whole document ---	1-14

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 November 1998	25/11/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Scarponi, U

2

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/CA 98/00773

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 280 571 A (ELI LILLY AND CO.,U.S.A.) 31 August 1988 see page 3, line 1 see claims 1,5 see examples	1-14
A,P	WO 98 22091 A (YISSUM RES. DEV. CO.,IL) 28 May 1998 see claims 1,3,9-11,13,14,16-21	1-14
A,P	EP 0 821 965 A (BASF) 4 February 1998 see claims 1,6 see page 7, line 25 - line 48	1-14

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/CA 98/00773

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 757991 A	12-02-1997	IT MI951716 A	03-02-1997
		AU 6083396 A	06-02-1997
		BR 9603270 A	28-04-1998
		CA 2179359 A	04-02-1997
		CN 1147516 A	16-04-1997
		FI 962937 A	04-02-1997
		JP 9104685 A	22-04-1997
		US 5677443 A	14-10-1997
FR 2549837 A	01-02-1985	AT 392470 B	10-04-1991
		AU 582121 B	16-03-1989
		AU 3125684 A	31-01-1985
		AU 634965 B	11-03-1993
		AU 3660189 A	05-10-1989
		BE 900241 A	28-01-1985
		CA 1265511 A	06-02-1990
		CH 662121 A	15-09-1987
		DE 3427828 A	14-02-1985
		DK 366684 A,B,	30-01-1985
		FI 843011 A,B,	30-01-1985
		GB 2145409 A,B	27-03-1985
		IE 57726 B	24-03-1993
		JP 1892249 C	26-12-1994
		JP 6013526 B	23-02-1994
		JP 60075484 A	27-04-1985
		NL 8402372 A	18-02-1985
		PT 78985 B	23-10-1986
		SE 463263 B	29-10-1990
		SE 8403897 A	30-01-1985
EP 107276 A	02-05-1984	AT 382154 B	26-01-1987
		AT 276783 A	15-06-1986
		AU 566881 B	05-11-1987
		AU 1741783 A	02-02-1984
		BE 897422 A	30-01-1984
		CA 1240313 A	09-08-1988
		CH 657134 A	15-08-1986
		CZ 280528 B	14-02-1996
		CS 8305687 A	15-03-1988
		CY 1434 A	02-09-1988

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interr ial Application No
PCT/CA 98/00773

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 107276 A		DE 3327449	A	02-02-1984
		DE 3374010	A	12-11-1987
		DK 68392	A	25-05-1992
		DK 349083	A,B,	31-01-1984
		FI 832757	A,B,	31-01-1984
		FR 2531087	A	03-02-1984
		GB 2127401	A,B	11-04-1984
		GR 79349	A	22-10-1984
		HK 84288	A	28-10-1988
		IE 55748	B	02-01-1991
		JP 2025666	C	26-02-1996
		JP 7030084	B	05-04-1995
		JP 59044391	A	12-03-1984
		KE 3805	A	03-06-1988
		LU 84935	A	23-11-1983
		NL 8302705	A	16-02-1984
		PT 77135	B	24-01-1986
		SE 453195	B	18-01-1988
		SE 8304208	A	31-01-1984
		SI 8311558	A	31-12-1995
		SK 403191	A	11-07-1995
		SU 1266471	A	23-10-1986
		US 4994567	A	19-02-1991
		US 5013833	A	07-05-1991
		US 4562181	A	31-12-1985
		US 4820833	A	11-04-1989
		ZA 8305579	A	26-09-1984
GB 2181052 A	15-04-1987	AT 393081	B	12-08-1991
		AT 260986	A	15-01-1991
		AU 594082	B	01-03-1990
		AU 6323286	A	02-04-1987
		BE 905518	A	30-03-1987
		CA 1282331	A	02-04-1991
		CH 672736	A	29-12-1989
		CY 1563	A	17-05-1991
		DE 3633292	A	09-04-1987
		DK 462486	A	31-03-1987
		EP 0223365	A	27-05-1987
		FR 2591597	A	19-06-1987

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern al Application No
PCT/CA 98/00773

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
GB 2181052 A		GR	862464 A	02-02-1987
		HK	84990 A	25-10-1990
		IE	59089 B	12-01-1994
		JP	2661662 B	08-10-1997
		JP	62123118 A	04-06-1987
		KR	9400233 B	12-01-1994
		LU	86613 A	05-04-1988
		NL	8602466 A	16-04-1987
		NO	173636 C	12-01-1994
		PH	25702 A	18-09-1991
		PT	83459 B	12-05-1989
		SE	8604114 A	31-03-1987
		US	4897270 A	30-01-1990
GB 2204792 A	23-11-1988	AT	393794 B	10-12-1991
		AU	607996 B	21-03-1991
		AU	1615788 A	17-11-1988
		BE	1000956 A	23-05-1989
		CA	1328405 A	12-04-1994
		CH	675357 A	28-09-1990
		CS	9104033 A	12-08-1992
		CY	1600 A	03-04-1992
		DE	3816464 A	24-11-1988
		DK	263288 A	15-11-1988
		FI	882253 A,B,	15-11-1988
		FR	2615101 A	18-11-1988
		GR	88100317 A,B	23-02-1989
		HK	106191 A	03-01-1992
		HR	940557 A	31-08-1997
		IE	61693 B	16-11-1994
		JP	2049587 C	10-05-1996
		JP	7078023 B	23-08-1995
		JP	63303928 A	12-12-1988
		KR	9509097 B	14-08-1995
		MX	11486 A	01-09-1993
		NL	8801236 A	01-12-1988
		NO	176695 B	06-02-1995
		PH	26015 A	29-01-1992
		PT	87474 B	30-09-1992
		SE	466047 B	09-12-1991

INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Intern... Application No
PCT/CA 98/00773

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2204792 A		SE 8801813 A	15-11-1988
		SI 8810927 A	28-02-1997
		SK 277898 B	11-07-1995
		SU 1837876 A	30-08-1993
		US 4865851 A	12-09-1989
EP 280571 A	31-08-1988	AU 604849 B	03-01-1991
		AU 1219388 A	01-09-1988
		CA 1316110 A	13-04-1993
		CN 1023765 B	16-02-1994
		CY 1741 A	17-02-1995
		DE 3882739 A	16-09-1993
		DE 3882739 T	17-02-1994
		DK 98088 A	28-08-1988
		EG 18523 A	30-04-1993
		ES 2044825 T	16-01-1994
		GR 93300027 T	24-05-1993
		HK 125793 A	19-11-1993
		IE 61419 B	02-11-1994
		JP 2092786 C	18-09-1996
		JP 8002793 B	17-01-1996
		JP 63227519 A	21-09-1988
		KR 9605140 B	22-04-1996
		LV 10184 A,B	20-10-1994
		MX 10558 A	01-11-1993
		PT 86831 B	29-05-1992
		SU 1831337 A	30-07-1993
		US 4968508 A	06-11-1990
WO 9822091 A	28-05-1998	AU 4882597 A	10-06-1998
EP 821965 A	04-02-1998	DE 19631085 A	05-02-1998
		CN 1176138 A	18-03-1998
		JP 10067686 A	10-03-1998

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K31/545 A61K9/14 A61K9/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 757 991 A (ACS DOBFAR S.P.A.,MILAN (IT)) 12 February 1997 see the whole document	1-14
A	FR 2 549 837 A (GLAXO) 1 February 1985 see the whole document	1-14
A	EP 0 107 276 A (GLAXO) 2 May 1984 cited in the application see claims see page 23, line 1 - line 32	1-14
A	GB 2 181 052 A (GLAXO) 15 April 1987 cited in the application see the whole document	1-14
A	GB 2 204 792 A (GLAXO) 23 November 1988 see the whole document	1-14

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 November 1998	25/11/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Scarponi, U

2

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 98/00773

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 280 571 A (ELI LILLY AND CO.,U.S.A.) 31 August 1988 see page 3, line 1 see claims 1,5 see examples	1-14
A,P	WO 98 22091 A (YISSUM RES. DEV. CO.,IL) 28 May 1998 see claims 1,3,9-11,13,14,16-21	1-14
A,P	EP 0 821 965 A (BASF) 4 February 1998 see claims 1,6 see page 7, line 25 - line 48	1-14

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 757991 A	12-02-1997	IT MI951716 A	03-02-1997
		AU 6083396 A	06-02-1997
		BR 9603270 A	28-04-1998
		CA 2179359 A	04-02-1997
		CN 1147516 A	16-04-1997
		FI 962937 A	04-02-1997
		JP 9104685 A	22-04-1997
		US 5677443 A	14-10-1997
FR 2549837 A	01-02-1985	AT 392470 B	10-04-1991
		AU 582121 B	16-03-1989
		AU 3125684 A	31-01-1985
		AU 634965 B	11-03-1993
		AU 3660189 A	05-10-1989
		BE 900241 A	28-01-1985
		CA 1265511 A	06-02-1990
		CH 662121 A	15-09-1987
		DE 3427828 A	14-02-1985
		DK 366684 A,B,	30-01-1985
		FI 843011 A,B,	30-01-1985
		GB 2145409 A,B	27-03-1985
		IE 57726 B	24-03-1993
		JP 1892249 C	26-12-1994
		JP 6013526 B	23-02-1994
		JP 60075484 A	27-04-1985
		NL 8402372 A	18-02-1985
		PT 78985 B	23-10-1986
		SE 463263 B	29-10-1990
		SE 8403897 A	30-01-1985
EP 107276 A	02-05-1984	AT, 382154 B	26-01-1987
		AT 276783 A	15-06-1986
		AU 566881 B	05-11-1987
		AU 1741783 A	02-02-1984
		BE 897422 A	30-01-1984
		CA 1240313 A	09-08-1988
		CH 657134 A	15-08-1986
		CZ 280528 B	14-02-1996
		CS 8305687 A	15-03-1988
		CY 1434 A	02-09-1988

INTERNAT. NAL SEARCH REPORT

Information on patent family members

Interr ial Application No
PCT/CA 98/00773

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 107276 A		DE 3327449 A	02-02-1984
		DE 3374010 A	12-11-1987
		DK 68392 A	25-05-1992
		DK 349083 A,B,	31-01-1984
		FI 832757 A,B,	31-01-1984
		FR 2531087 A	03-02-1984
		GB 2127401 A,B	11-04-1984
		GR 79349 A	22-10-1984
		HK 84288 A	28-10-1988
		IE 55748 B	02-01-1991
		JP 2025666 C	26-02-1996
		JP 7030084 B	05-04-1995
		JP 59044391 A	12-03-1984
		KE 3805 A	03-06-1988
		LU 84935 A	23-11-1983
		NL 8302705 A	16-02-1984
		PT 77135 B	24-01-1986
		SE 453195 B	18-01-1988
		SE 8304208 A	31-01-1984
		SI 8311558 A	31-12-1995
		SK 403191 A	11-07-1995
		SU 1266471 A	23-10-1986
		US 4994567 A	19-02-1991
		US 5013833 A	07-05-1991
		US 4562181 A	31-12-1985
		US 4820833 A	11-04-1989
		ZA 8305579 A	26-09-1984
GB 2181052 A	15-04-1987	AT 393081 B	12-08-1991
		AT 260986 A	15-01-1991
		AU 594082 B	01-03-1990
		AU 6323286 A	02-04-1987
		BE 905518 A	30-03-1987
		CA 1282331 A	02-04-1991
		CH 672736 A	29-12-1989
		CY 1563 A	17-05-1991
		DE 3633292 A	09-04-1987
		DK 462486 A	31-03-1987
		EP 0223365 A	27-05-1987
		FR 2591597 A	19-06-1987

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2181052 A		GR 862464 A	02-02-1987
		HK 84990 A	25-10-1990
		IE 59089 B	12-01-1994
		JP 2661662 B	08-10-1997
		JP 62123118 A	04-06-1987
		KR 9400233 B	12-01-1994
		LU 86613 A	05-04-1988
		NL 8602466 A	16-04-1987
		NO 173636 C	12-01-1994
		PH 25702 A	18-09-1991
		PT 83459 B	12-05-1989
		SE 8604114 A	31-03-1987
		US 4897270 A	30-01-1990
GB 2204792 A	23-11-1988	AT 393794 B	10-12-1991
		AU 607996 B	21-03-1991
		AU 1615788 A	17-11-1988
		BE 1000956 A	23-05-1989
		CA 1328405 A	12-04-1994
		CH 675357 A	28-09-1990
		CS 9104033 A	12-08-1992
		CY 1600 A	03-04-1992
		DE 3816464 A	24-11-1988
		DK 263288 A	15-11-1988
		FI 882253 A,B,	15-11-1988
		FR 2615101 A	18-11-1988
		GR 88100317 A,B	23-02-1989
		HK 106191 A	03-01-1992
		HR 940557 A	31-08-1997
		IE 61693 B	16-11-1994
		JP 2049587 C	10-05-1996
		JP 7078023 B	23-08-1995
		JP 63303928 A	12-12-1988
		KR 9509097 B	14-08-1995
		MX 11486 A	01-09-1993
		NL 8801236 A	01-12-1988
		NO 176695 B	06-02-1995
		PH 26015 A	29-01-1992
		PT 87474 B	30-09-1992
		SE 466047 B	09-12-1991

INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Internat...l Application No
PCT/CA 98/00773

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2204792 A		SE 8801813 A	15-11-1988
		SI 8810927 A	28-02-1997
		SK 277898 B	11-07-1995
		SU 1837876 A	30-08-1993
		US 4865851 A	12-09-1989
EP 280571 A	31-08-1988	AU 604849 B	03-01-1991
		AU 1219388 A	01-09-1988
		CA 1316110 A	13-04-1993
		CN 1023765 B	16-02-1994
		CY 1741 A	17-02-1995
		DE 3882739 A	16-09-1993
		DE 3882739 T	17-02-1994
		DK 98088 A	28-08-1988
		EG 18523 A	30-04-1993
		ES 2044825 T	16-01-1994
		GR 93300027 T	24-05-1993
		HK 125793 A	19-11-1993
		IE 61419 B	02-11-1994
		JP 2092786 C	18-09-1996
		JP 8002793 B	17-01-1996
		JP 63227519 A	21-09-1988
		KR 9605140 B	22-04-1996
		LV 10184 A,B	20-10-1994
		MX 10558 A	01-11-1993
		PT 86831 B	29-05-1992
		SU 1831337 A	30-07-1993
		US 4968508 A	06-11-1990
WO 9822091 A	28-05-1998	AU 4882597 A	10-06-1998
EP 821965 A	04-02-1998	DE 19631085 A	05-02-1998
		CN 1176138 A	18-03-1998
		JP 10067686 A	10-03-1998

PATENT COOPERATION TREATY

PCT

REC'D 31 MAY 1999
WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PCT-1034		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA98/00773	07/08/1998	15/08/1997
International Patent Classification (IPC) or national classification and IPC		
A61K31/545		
Applicant		
SHERMAN, Bernard, Charles		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report
   II ☐ Priority
   III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   IV ☐ Lack of unity of invention
   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   VI ☐ Certain documents cited
   VII ☐ Certain defects in the international application
   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10/03/1999	27.05.99
Name and mailing address of the international preliminary examining authority:	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0 Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Giacobbe, S Telephone No. (+49-89) 2399

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA98/00773

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-8 as originally filed

Claims, No.:

1-14 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

see separate sheet

1. Section V

1.1 Cited Documents

The following documents (D) are referred to in this communication:

D1: EP-A-0 757 991 (ACS DOBFAR S.P.A.,MILAN (IT)) 12 February 1997
D2: FR-A-2 549 837 (GLAXO) 1 February 1985
D3: EP-A-0 107 276 (GLAXO) 2 May 1984 cited in the application
D4: GB-A-2 181 052 (GLAXO) 15 April 1987 cited in the application
D5: GB-A-2 204 792 (GLAXO) 23 November 1988
D6: EP-A-0 280 571 (ELI LILLY AND CO.,U.S.A.) 31 August 1988
D7: WO 98 22091 A (YISSUM RES. DEV. CO.,IL) 28 May 1998
D8: EP-A-0 821 965 (BASF) 4 February 1998

1.2 Art 33(2) PCT (Novelty)

The present application meets the requirements of Article 33(2) PCT, because the subject-matter of claims 1-14 is new.

The subject-matter of independent claim is new because the previous art documents D1-D8 do not disclose any co-precipitate of cefuroxime axetil and a water-soluble excipient. The co-precipitate being new, also the process for making it and compositions containing it are new.

1.3 Art 33(3) PCT (Inventive step)

The present application does meet the requirements of Article 33(3) PCT, because the subject-matter of claims 1-14 does involve an inventive step.

The technical problem which the present application sought to solve vis-à-vis any of the prior art documents D1-D8 is *"how to find an alternative bioavailable formulation of cefuroxime axetil"*. The solution proposed, i.e. the co-precipitation of cefuroxime axetil with a water-soluble excipient, cannot be derived from such documents by the person skilled in the art without the exercise of inventive abilities and therefore it involves an inventive step.

TENT COOPERATION TREATY

09/485558

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
PCT-1034		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 98/ 00773	07/08/1998	15/08/1997
Applicant		
SHERMAN, Bernard, Charles		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [ ] **Certain claims were found unsearchable** (see Box I).

2. [ ] **Unity of invention is lacking** (see Box II).

3. [ ] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - [ ] filed with the international application.
   - [ ] furnished by the applicant separately from the international application,
     - [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - [ ] Transcribed by this Authority

4. With regard to the **title,**
   - [X] the text is approved as submitted by the applicant
   - [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   - [X] the text is approved as submitted by the applicant
   - [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

   Figure No. _____
   - [ ] as suggested by the applicant.
   - [ ] because the applicant failed to suggest a figure.
   - [ ] because this figure better characterizes the invention.
   - [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 98/00773

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K31/545 A61K9/14 A61K9/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 757 991 A (ACS DOBFAR S.P.A.,MILAN (IT)) 12 February 1997 see the whole document ---	1-14
A	FR 2 549 837 A (GLAXO) 1 February 1985 see the whole document ---	1-14
A	EP 0 107 276 A (GLAXO) 2 May 1984 cited in the application see claims see page 23, line 1 - line 32 ---	1-14
A	GB 2 181 052 A (GLAXO) 15 April 1987 cited in the application see the whole document ---	1-14
A	GB 2 204 792 A (GLAXO) 23 November 1988 see the whole document ---	1-14

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 November 1998	25/11/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Scarponi, U

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 280 571 A (ELI LILLY AND CO.,U.S.A.) 31 August 1988 see page 3, line 1 see claims 1,5 see examples	1-14
A,P	WO 98 22091 A (YISSUM RES. DEV. CO.,IL) 28 May 1998 see claims 1,3,9-11,13,14,16-21	1-14
A,P	EP 0 821 965 A (BASF) 4 February 1998 see claims 1,6 see page 7, line 25 - line 48	1-14

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/CA 98/00773

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 757991 A	12-02-1997	IT MI951716 A	03-02-1997
		AU 6083396 A	06-02-1997
		BR 9603270 A	28-04-1998
		CA 2179359 A	04-02-1997
		CN 1147516 A	16-04-1997
		FI 962937 A	04-02-1997
		JP 9104685 A	22-04-1997
		US 5677443 A	14-10-1997
FR 2549837 A	01-02-1985	AT 392470 B	10-04-1991
		AU 582121 B	16-03-1989
		AU 3125684 A	31-01-1985
		AU 634965 B	11-03-1993
		AU 3660189 A	05-10-1989
		BE 900241 A	28-01-1985
		CA 1265511 A	06-02-1990
		CH 662121 A	15-09-1987
		DE 3427828 A	14-02-1985
		DK 366684 A,B,	30-01-1985
		FI 843011 A,B,	30-01-1985
		GB 2145409 A,B	27-03-1985
		IE 57726 B	24-03-1993
		JP 1892249 C	26-12-1994
		JP 6013526 B	23-02-1994
		JP 60075484 A	27-04-1985
		NL 8402372 A	18-02-1985
		PT 78985 B	23-10-1986
		SE 463263 B	29-10-1990
		SE 8403897 A	30-01-1985
EP 107276 A	02-05-1984	AT 382154 B	26-01-1987
		AT 276783 A	15-06-1986
		AU 566881 B	05-11-1987
		AU 1741783 A	02-02-1984
		BE 897422 A	30-01-1984
		CA 1240313 A	09-08-1988
		CH 657134 A	15-08-1986
		CZ 280528 B	14-02-1996
		CS 8305687 A	15-03-1988
		CY 1434 A	02-09-1988

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 107276 A		DE 3327449 A	02-02-1984
		DE 3374010 A	12-11-1987
		DK 68392 A	25-05-1992
		DK 349083 A,B,	31-01-1984
		FI 832757 A,B,	31-01-1984
		FR 2531087 A	03-02-1984
		GB 2127401 A,B	11-04-1984
		GR 79349 A	22-10-1984
		HK 84288 A	28-10-1988
		IE 55748 B	02-01-1991
		JP 2025666 C	26-02-1996
		JP 7030084 B	05-04-1995
		JP 59044391 A	12-03-1984
		KE 3805 A	03-06-1988
		LU 84935 A	23-11-1983
		NL 8302705 A	16-02-1984
		PT 77135 B	24-01-1986
		SE 453195 B	18-01-1988
		SE 8304208 A	31-01-1984
		SI 8311558 A	31-12-1995
		SK 403191 A	11-07-1995
		SU 1266471 A	23-10-1986
		US 4994567 A	19-02-1991
		US 5013833 A	07-05-1991
		US 4562181 A	31-12-1985
		US 4820833 A	11-04-1989
		ZA 8305579 A	26-09-1984
GB 2181052 A	15-04-1987	AT 393081 B	12-08-1991
		AT 260986 A	15-01-1991
		AU 594082 B	01-03-1990
		AU 6323286 A	02-04-1987
		BE 905518 A	30-03-1987
		CA 1282331 A	02-04-1991
		CH 672736 A	29-12-1989
		CY 1563 A	17-05-1991
		DE 3633292 A	09-04-1987
		DK 462486 A	31-03-1987
		EP 0223365 A	27-05-1987
		FR 2591597 A	19-06-1987

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2181052 A		GR 862464 A	02-02-1987
		HK 84990 A	25-10-1990
		IE 59089 B	12-01-1994
		JP 2661662 B	08-10-1997
		JP 62123118 A	04-06-1987
		KR 9400233 B	12-01-1994
		LU 86613 A	05-04-1988
		NL 8602466 A	16-04-1987
		NO 173636 C	12-01-1994
		PH 25702 A	18-09-1991
		PT 83459 B	12-05-1989
		SE 8604114 A	31-03-1987
		US 4897270 A	30-01-1990
GB 2204792 A	23-11-1988	AT 393794 B	10-12-1991
		AU 607996 B	21-03-1991
		AU 1615788 A	17-11-1988
		BE 1000956 A	23-05-1989
		CA 1328405 A	12-04-1994
		CH 675357 A	28-09-1990
		CS 9104033 A	12-08-1992
		CY 1600 A	03-04-1992
		DE 3816464 A	24-11-1988
		DK 263288 A	15-11-1988
		FI 882253 A,B,	15-11-1988
		FR 2615101 A	18-11-1988
		GR 88100317 A,B	23-02-1989
		HK 106191 A	03-01-1992
		HR 940557 A	31-08-1997
		IE 61693 B	16-11-1994
		JP 2049587 C	10-05-1996
		JP 7078023 B	23-08-1995
		JP 63303928 A	12-12-1988
		KR 9509097 B	14-08-1995
		MX 11486 A	01-09-1993
		NL 8801236 A	01-12-1988
		NO 176695 B	06-02-1995
		PH 26015 A	29-01-1992
		PT 87474 B	30-09-1992
		SE 466047 B	09-12-1991

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2204792 A		SE 8801813 A	15-11-1988
		SI 8810927 A	28-02-1997
		SK 277898 B	11-07-1995
		SU 1837876 A	30-08-1993
		US 4865851 A	12-09-1989
EP 280571 A	31-08-1988	AU 604849 B	03-01-1991
		AU 1219388 A	01-09-1988
		CA 1316110 A	13-04-1993
		CN 1023765 B	16-02-1994
		CY 1741 A	17-02-1995
		DE 3882739 A	16-09-1993
		DE 3882739 T	17-02-1994
		DK 98088 A	28-08-1988
		EG 18523 A	30-04-1993
		ES 2044825 T	16-01-1994
		GR 93300027 T	24-05-1993
		HK 125793 A	19-11-1993
		IE 61419 B	02-11-1994
		JP 2092786 C	18-09-1996
		JP 8002793 B	17-01-1996
		JP 63227519 A	21-09-1988
		KR 9605140 B	22-04-1996
		LV 10184 A,B	20-10-1994
		MX 10558 A	01-11-1993
		PT 86831 B	29-05-1992
		SU 1831337 A	30-07-1993
		US 4968508 A	06-11-1990
WO 9822091 A	28-05-1998	AU 4882597 A	10-06-1998
EP 821965 A	04-02-1998	DE 19631085 A	05-02-1998
		CN 1176138 A	18-03-1998
		JP 10067686 A	10-03-1998